WEST Search History

DATE: Saturday, March 29, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR		
L5	L4 and acid$4 adj6 ph	181	L5
L4	L3 and (asp or aspartic)adj4 (glu or glutamic or lys or lysine)	741	L4
L3	L2 and stab$8	1418	L3
L2	L1 and (site or point)adj4 (mutat$6 or substit$8 or add$8)	1543	L2
L1	fibronectin	8552	L1

END OF SEARCH HISTORY

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     FILE 'CA' ENTERED AT 12:25:28 ON 29 MAR 2003
L1         16908 S FIBRONECTIN
L2             4 S L1 AND ASP(4W)7
L3             2 S L1 AND FN10
L4          1008 S L1 AND MUT?
L5           453 S L4 AND SUB?
L6            56 S L5 AND STAB?
L7            46 S L6 NOT 2002-2003/PY

     FILE 'MEDLINE' ENTERED AT 12:29:16 ON 29 MAR 2003
L8         19578 S L1
L9             1 S L2
L10            0 S L3
L11         1129 S L4
L12          523 S L5
L13           60 S L6
L14           11 S L13 NOT L7

     FILE 'BIOSIS' ENTERED AT 12:30:25 ON 29 MAR 2003
L15        26315 S L1
L16            3 S L2
L17            3 S L16 NOT L3

=> s l6
         26315 FIBRONECTIN
        473020 MUT?
       2176284 SUB?
        356944 STAB?
L18        57 L5 AND STAB?

=> s l7
         26315 FIBRONECTIN
        473020 MUT?
       2176284 SUB?
        356944 STAB?
        547509 2002-2003/PY
L19        46 L6 NOT 2002-2003/PY

=> s l19 not l7
         26315 FIBRONECTIN
        473020 MUT?
       2176284 SUB?
        356944 STAB?
        547509 2002-2003/PY
L20         0 L19 NOT L7
```

L2 ANSWER 1 OF 4 CA COPYRIGHT 2003 ACS

TI Stabilization of a **fibronectin** type III domain by the removal of unfavorable electrostatic interactions on the protein surface

AU Koide, Akiko; Jordan, Michael R.; Horner, Scott R.; Batori, Vincent; Koide, Shohei

SO Biochemistry (2001), 40(34), 10326-10333
CODEN: BICHAW; ISSN: 0006-2960

PY 2001

AB It is generally considered that electrostatic interactions on the protein surface, such as ion pairs, contribute little to protein stability, although they may play important roles in conformational specificity. The authors found that the tenth **fibronectin** type III domain of human **fibronectin** (FNfn10) is more stable at acidic pH than neutral pH, with an apparent midpoint of transition near pH 4. Detn. of pKa's for all the side chain carboxyl groups of Asp and Glu residues revealed that Asp 23 and Glu 9 have an upshifted pKa. These residues and **Asp 7** form a neg. charged patch on the surface of FNfn10, with **Asp 7** centrally located between Asp 23 and Glu 9, suggesting repulsive electrostatic interactions among these residues at neutral pH. Mutant proteins, D7N and D7K, in which **Asp 7** was replaced with Asn and Lys, resp., exhibited a modest but significant increase in stability at neutral pH, compared to the wild type, and they no longer showed pH dependence of stability. The pKa's of Asp 23 and Glu 9 in these mutant proteins shifted closer to their resp. unperturbed values, indicating that the unfavorable electrostatic interactions have been reduced in the mutant proteins. Interestingly, the wild-type and mutant proteins were all stabilized to a similar degree by the addn. of 1 M sodium chloride at both neutral and acidic pH, suggesting that the repulsive interactions between the carboxyl groups cannot be effectively shielded by 1 M sodium chloride. These results indicate that repulsive interactions between like charges on the protein surface can destabilize a protein, and protein stability can be significantly improved by relieving these interactions.